

## **Meningococcal**

In this segment of the program we will briefly discuss meningococcal disease and meningococcal vaccine. This vaccine was previously of greatest interest to travel health providers. But there has been more general interest recently in the context of vaccination of young adults, particularly college students. The meningococcal chapter in your text begins on page 247.

Meningococcal disease is an acute, potentially severe illness caused by the bacteria *Neisseria meningitidis*. *Neisseria meningitidis* is a leading cause of bacterial meningitis and sepsis in many parts of the world. Meningococcal disease is unique among causes of bacterial meningitis in that it causes not only sporadic disease but also outbreaks. In sub-Saharan Africa the organism causes major epidemics of meningitis and bacteremia. The World Health Organization estimated meningococcal disease was the cause of 171,000 deaths worldwide in 2000.

*Neisseria meningitidis*, or meningococcus, is an aerobic gram-negative bacterium, closely related to *Neisseria gonorrhea*, and to several nonpathogenic *Neisseria* species. Meningococci are classified into groups, called serogroups, based on the characteristics of the polysaccharide capsule. At least 13 antigenically and chemically distinct polysaccharide capsules have been described. However, most invasive disease is caused by one of five serogroups: A, B, C, Y, and W-135.

The relative importance of each serogroup depends on geographic location, as well as other factors, such as age. For instance, serogroup A is a major cause of disease in sub-Saharan Africa, but is rarely isolated in the United States.

The incubation period of meningococcal disease is short – 3 to 4 days, with a range of 2 to 10 days. Meningococcal disease can have a variety of manifestations. Meningitis is the most common presentation and represents about half of all reported cases of invasive meningococcal disease. Meningeal infection is similar to other forms of acute purulent meningitis, with sudden onset of fever, headache, and stiff neck. Meningococcal sepsis, or meningococcemia may occur without meningitis. This condition is characterized by abrupt onset of fever and a petechial or purpuric rash, often associated with hypotension, shock, acute adrenal hemorrhage, and multiorgan failure. Less common presentations of meningococcal disease include pneumonia, arthritis, otitis media, and epiglottitis.

The case fatality rate of invasive meningococcal disease is 9% to 12%, even with appropriate antibiotic therapy. The fatality rate of meningococcemia is up to 40%.

Up to 20% of survivors have permanent sequelae, such as hearing loss, neurologic damage, or loss of a limb.

Even in the absence of a routine vaccination program, meningococcal disease is relatively rare in the United States, with 2,000 to 3,000 cases reported each year. The overall rate in the United States is about 1 case per 100,000 population, shown here in the red line. The highest age specific rates are among infants younger than 1 year of age. Incidence declines in early childhood, increases during adolescence and early adulthood, declines among older adults, increasing again among the elderly. Although incidence is relatively low, more cases occur in persons 23-64 years of age than in any other age group.

The proportion of disease caused by different serogroups has changed during the last 15 years. From 1988 to 1991, most cases of meningococcal disease in the United States were due to either serogroup C or B, and serogroup Y accounted for only 2% of cases. In 1996 through 2001, serogroup Y accounted for 21% of cases, with serogroups C and B accounting for 42% and 31%, respectively. Serogroups A and W-135 are rare causes of invasive disease in the U.S. The proportion of cases caused by each serogroup varies by age group. In 2001, 65% of cases among infants aged <1 year were caused by serogroup B, for which no vaccine is available in the United States.

Risk factors for the development of meningococcal disease include deficiencies in the terminal complement pathway and functional or anatomic asplenia. Persons with HIV infection are probably at increased risk for meningococcal disease. In the African “meningitis belt”, an area that extends from Ethiopia to Senegal, seasonal peaks of meningococcal disease occur with rates several fold higher than in industrialized countries. In addition, epidemics occur every 8 to 12 years with attack rates of 500 to 1,000 cases per 100,000 population.

In the United States, more than 95% of cases of meningococcal disease are sporadic single cases. But meningococcal disease sometimes occurs in small outbreaks, generally among groups in closed settings. Outbreaks have occurred among college students, and led to concerns that this group might be at increased risk for the disease. Surveillance for meningococcal disease among college students in the United States was started in 1998.

This graphic shows the incidence rate of meningococcal disease among various groups of 18 to 23 year olds in 1998 and 1999. The overall incidence among 18 to 23 year olds, including those who are not college students, was 1.4 cases per 100,000 population – not much different than the overall U.S. rate. Among college freshmen, the rate was slightly higher, 1.9 per 100,000. But among college freshmen who live in dormitories, the rate was 5.1 per 100,000, more than twice as high as for all freshmen, and three times the rate for people of the same age who do not attend college. A case control study among college students with meningococcal disease found that being a freshman living in a dormitory, white race, radiator heat, and recent upper respiratory infection were

also risk factors for the disease. Interestingly, attending a movie in the prior month **reduced** the risk.

The only meningococcal vaccine currently available in the United States is produced by Aventis Pasteur with the brand name Menomune. It is a quadrivalent vaccine that contains the capsular polysaccharide of meningococcal serogroups A, C, Y, and W-135. As we mentioned earlier, serogroups C and Y account for about 65% of disease in the United States. Serogroups A and W-135 are rare in the U.S. No vaccine is available for serotype B, which is responsible for about a third of meningococcal disease in this country. Like other pure polysaccharide vaccines, meningococcal vaccine is not effective in children younger than 18 months of age. The schedule is one dose with revaccination in 3 to 5 years if the person remains at risk. We will discuss revaccination in more detail in a moment.

Serogroup A and C vaccines have been found to reduce disease incidence by 85% to 95%. Clinical protection from Y and W-135 serogroups has not been determined directly. But immunogenicity, as measured by an antibody response, has been demonstrated in older children and adults. The duration of vaccine-induced immunity is not known with certainty. Among infants and children younger than 5 years of age, antibodies against serogroup A and C polysaccharides decrease substantially during the first 3 years following a single dose of vaccine. In healthy adults, antibody levels also decrease, but antibodies are detectable as long as 10 years after vaccination. Vaccine induced protection probably persists in older children and adults for at least 3 years.

Meningococcal polysaccharide is not recommended for routine vaccination of civilians in the United States. ACIP recommends meningococcal vaccine only for certain high risk persons. Risk factors for meningococcal disease include terminal complement component deficiency and functional or anatomic asplenia. In addition, ACIP recommends the vaccine be considered for certain research and laboratory personnel, particularly those who are exposed routinely to meningococci in solutions that may be aerosolized. Vaccine should also be considered for travelers to and U.S. citizens residing in countries in which *Neisseria meningitidis* is hyperendemic or epidemic, such as the central African meningitis belt and the Hajj in Saudi Arabia.

In 1997, the American College Health Association recommended that college students should consider vaccination to reduce their risk of meningococcal disease. ACIP has also considered this issue at length. The most recent ACIP statement on meningococcal vaccine, and a specific statement addressing vaccination of college students was published in June 2000. ACIP does not recommend routine meningococcal vaccination for college students. ACIP recommends that providers inform students – particularly freshmen living in dormitories – about meningococcal disease and the benefits of vaccination. If a college student or their parent requests meningococcal vaccine, the provider should administer the vaccine, or direct the student to a site where vaccine is

available, such as a college health service. Many travel health clinics also stock meningococcal vaccine. You should be aware that some states and colleges are now **requiring** meningococcal vaccine for incoming freshmen students. Hopefully, this requirement will be provided in the student's prematriculation information, so it will not come as a surprise when they arrive for their first day of class.

We receive many questions about revaccination with meningococcal polysaccharide vaccine. As with other pure polysaccharide vaccines, there is little benefit of more than one dose. Although there are few data to support revaccination, a second dose may be indicated for persons at high risk for infection, such as persons residing in areas in which the disease is epidemic. Providers should consider revaccination of children who were first vaccinated when they were younger than 4 years of age after 2 to 3 years, if the child remains at high risk. Although the need for revaccination of older children and adults has not been determined, antibody levels rapidly decline after 2 to 3 years, and if an indication still exists for vaccination, revaccination may be considered 3 to 5 years after receipt of the first dose. There is currently no indication for more than one revaccination dose. Continued attendance of college, or continued residence in a college dormitory is **not** an indication for revaccination in the absence of another indication, such as asplenia.

Adverse reactions following meningococcal vaccine are generally mild. The most frequent are local reactions, such as erythema and pain at the site of injection. These reactions last for 1 or 2 days, and occur in 5% to 10% of recipients. Low grade fever occurs in less than 2% of vaccinated children. Fever is less frequent in older persons. Severe reactions to meningococcal vaccine are rare.

Contraindications and precautions for meningococcal vaccine are the same as those for most other inactivated vaccines. A severe allergic reaction to a vaccine component or following a prior dose is a contraindication to receipt of further doses. A moderate or severe acute illness is reason to defer routine vaccination. Pregnancy, breastfeeding, and immunosuppression are not contraindications to vaccination.

Meningococcal polysaccharide vaccine is not effective in children younger than 18 to 24 months of age. A meningococcal **conjugate** vaccine is needed to prevent disease in this age group. Several manufacturers are working on a meningococcal conjugate vaccine, which could be available in the United States as early as 2005.

A serogroup B vaccine is also needed. Serogroup B accounts for one third of invasive disease in the U.S., and 65% of invasive disease among children younger than 1 year of age. Development of a serogroup B vaccine has been difficult because antibodies to serogroup B polysaccharide cross react with certain proteins in human tissue. Although serogroup B vaccines are available in other countries, it is likely to be several years before such a vaccine is available in the U.S.